

**REMARKS**

Reconsideration and allowance are respectfully requested.

Claims 44-58 are now pending, with claim 44 being the sole independent claim.

Claims 1-43 have been cancelled without prejudice to or disclaimer of the subject matter recited therein.

Turning now to the Office Action mailed May 7, 2003:

Regarding the restriction requirement made final, the pending claims now recite only the elected SEQ ID NO:27 encoding SEQ ID NO:28.

Regarding the Sequence Listing, nucleotides 5-1057 (stop) of SEQ ID NO:27 encodes the 350 amino acid sequence of SEQ ID NO:28.

Regarding the Drawings, please enter the attached replacement sheets, as described above in the Amendments to the Drawings section.

Regarding the Specification Objections: Applicants have amended the specification to reflect the new figure numbering; regarding the statement in the specification at page 2, lines 3-4, Applicants intended this statement to mean that, because tocopherols are synthesized only in plants, the enzymes described herein are good targets for herbicides that will not affect animals.

Regarding the Section 112, 2d paragraph rejections, Applicants submit that now pending claims 44-58 obviate these rejections. Withdrawal of the Section 112, 2d paragraph rejections is respectfully requested.

Regarding the Section 112, 1<sup>st</sup> paragraph (written description) rejection, Applicants respectfully traverse.

First, Applicants submit that the specification discloses to one of ordinary skill in the art a representative number of gamma tocopherol methyltransferases with at least 80% sequence identity to SEQ ID NO:28, and not just a single polynucleotide encoding SEQ ID NO:28.

The specification at page 8, line 30 to page 9, line 4 discloses alterations in nucleotide sequence that are not expected to alter functionality, such as alterations that produce a chemically equivalent amino acid at a given site or alterations in the N- or C-terminal portions. Thus, from the foregoing, the skilled artisan would immediately understand the specification to disclose a representative number of polynucleotide sequences, having different nucleotide substitutions, that encode gamma tocopherol methyltransferases but that vary (within 80% sequence identity) of SEQ ID NO:28.

Second, under the PTO Written Description Guidelines, the written description requirement is met with disclosure of "functional characteristics when coupled with a

known or disclosed correlation between function and structure.” Guidelines, 66 Fed. Reg. at 1106.

Applicants submit in a Supplemental Information Disclosure Statement filed simultaneously herewith the following two references:

Kagan et al., *Archives of Biochemistry and Biophysics*, (1994) 310:417 – 427

Willcock et al., *EMBO J.*, (1994) 13: 3902-8

Kagan et al. discloses three sequence motifs (Motifs I, II, and III) that are conserved among 84 different S-adenosylmethionine-dependent methyltransferases. Kagan et al. suggest that these conserved regions contribute to the binding of the substrate S-adenosylmethionine and/or the product S-adenosylhomocysteine.<sup>1</sup>

Motif I occurs in 69 of the 84 methyltransferase sequences (29 distinct enzymes) and has a consensus sequence of (V/I/L)(L/V)(D/E)(V/I)G(G/C)G(T/P)G. According to Willcock et al., changes within this sequence motif I abolish S-adenosylmethionine binding.

Motif II is present in 46 of the 84 sequences (26 distinct enzymes) and has a consensus sequence of (P/G)/(Q/T)(F/Y/A)DA(I/V/Y)/(F/I)(C/V/L).

Motif III is present in 61 of the 84 sequences (28 distinct enzymes) and has a consensus sequence of LL(R/K)PGG(R/I/L)(L/I)(L/F/I/V)(I/L).

All three motifs are found in 45 of the 84 sequences, and an additional 15 have motifs I and III.

Gamma tocopherol methyltransferase uses S-adenosylmethionine as a methyl group donor.

Attached hereto as Appendix A is a comparison of SEQ ID NO:28 of the pending claims with gamma tocopherol methyltransferase sequences from *Synechocystis* sp. (SEQ ID NO:39 of the instant application; NCBI GI No. 1001725)

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<sup>1</sup> However, see also the following discussions in Kagan et al.:

- Page 419, column 2, first paragraph under Results.
- Page 422-23, “Methyltransferase sequence motifs in other AdoMet or AdoHcy-utilizing enzymes” section.
- Page 423, column 2, “Predictive potential of methyltransferase sequence motifs” section. But also see in this same section the statement that “None of the retrieved proteins, other than methyltransferases or putative methyltransferases, were found to contain more than one of the three sequence motifs.”
- Page 424, second column, first full paragraph (beginning with “Two other regions, termed motifs II and III...”), lines 1-6 in particular of that paragraph.
- Page 425, second column, first full paragraph (beginning with “Motif III is found at an interval...”), lines 12-13 in particular of that paragraph.
- Page 426, second column, first full paragraph (beginning with “There are, however, a number of...”).
- Page 427, first column, first two full paragraphs.

and *Arabidopsis thaliana* (SEQ ID NO:40 of the instant application; NCBI GI No. 4106538). See Tables 4 and 5 of the instant application.

Motifs I and III of Kagan et al. are shown underlined on Appendix A. SEQ ID NO:28 does not appear to have motif II. Amino acids conserved among all sequences are indicated with an asterisk (\*) on the top row; dashes are used by the program to maximize alignment of the sequences.

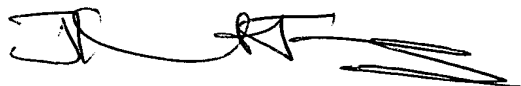
In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the Section 112, 1<sup>st</sup> paragraph (written description) rejection.

Applicants believe that the foregoing is responsive to each of the points recited in the Office Action, and submit that the present application is in allowable form. Favorable consideration and passage to issue are solicited.

The Commissioner is authorized to charge Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company) for any requisite fees due or to credit any overpayment.

Applicants' undersigned may be reached at the below-listed numbers.

Respectfully submitted,



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**APPENDIX A**  
**(Amendment and Response to Non-Final Office Action)**

\* \*  
gi-1001725 MVYHVRPKHALFLAFYCY-----FS-----LLTMASAT  
gi-4106538 MKATLAAP--SSLTSLPYRTNSS--FGSKSLLFRSPSSSSSVSMTTTRGNVAVAAAATS  
SEQ\_ID\_NO\_28 MATVVRIPTISCIHIHTFRSQSPRTFA-RIRVGPRSWAPIRASAASSERGEIVLEQPKK

\* \* \* \* \*  
gi-1001725 IASADLYEKIKNFYDDSSGLWEDVWGEHMHGYYGPHGTYRI--DRRQAQIDLIKELLA  
gi-4106538 TEA--LRKGIAEFYNETSGLWEEIWGDHMHGIFYDPDSSVQLSDSGHKEAQIRMIEESLR  
SEQ\_ID\_NO\_28 DDKKKLQKGIAEFYDESSGLWENIWGDHMHGIFYDSSTVSLSD--HRAAQIRMIQESLR

\* \* \* \* \*  
gi-1001725 WAVP---QNSAKPRKILDGCGIGGSSLYLAQQHQAQEVMGASLSPVQVERAGERARALGL  
gi-4106538 FAGVTDEEEKKIKKVVDVGCIGGSSRYLASKFGAECIGITLSPVQAKRANDLAAAQSL  
SEQ\_ID\_NO\_28 FASVS-EERSKWPKSIVDVGCGIGGSSRYLAKKFGATSVGITLSPVQAQRANALAAAQGL

Motif I  
\* \* \* \* \*  
gi-1001725 GSTCQFQVANALDLPFASDSFDWVWSLESGEHMPNKAQFLQEAWRVLKPGRILILATWCH  
gi-4106538 SHKASFQVADALDQPFEDGKFDLVWSMESGEHMPDKAKFVKELVRVAAPGGRIIIVTWCH  
SEQ\_ID\_NO\_28 ADKVSFQVADALQPPFSDGQFDLVWSMESGEHMPDKAKFVGELARVAAPGAIIVTWCH

Motif III  
\* \* \* \* \*  
gi-1001725 RPIDPGNGPLTADERRHLQAIYDVYCLPYVVSLLPDYEAIAARECGFGEIKTADWSVAVAPF  
gi-4106538 RNLSAGEEALQPWEQNILDKICKTFYLPWCSTDDYVNLLQSHSLQDIKCADWSENVAPF  
SEQ\_ID\_NO\_28 RDLGPDEQSLHPWEQDLLKKICDAYYLPWCSTSDYVKLLQSLSLQDIKSEDWSRFVAPF

\* \* \* \* \*  
gi-1001725 WDRVIESAFDPRVLWALGQAGPKIINAALCLRLMKWGYERGLVRFGLLTGIKPLV  
gi-4106538 WPAVIRTALTWKGLVSLLRSGMKSIGKALTMPLMIEGYKKGVIKFGIITCQKPL-  
SEQ\_ID\_NO\_28 WPAVIRSAFTWKGLSSLLSSGQKTIKALAMPLMIEGYKKDLIKFAIITCRKPE-